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Hyperemesis gravidarum and gestational transient hyperthyroidism: A case report

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Abstract: Gestational transient hyperthyroidism is often associated with hyperemesis gravidarum, which is a relatively uncommon condition in women during the first and second trimester of pregnancy. It is a transient phenomenon which resolves itself by the 20th gestational week. This is a report of a case of a pregnant woman with hyperemesis gravidarum and gestational transient hyperthyroidism who was admitted to a government hospital for 1 month.

Keywords: Hyperemesis Gravidarum, Gestational Transient Hyperthyroidism, Pregnancy

1. Introduction

Hyperemesis gravidarum (which occurs in 0.3-1% of pregnancies)[1] and gestational transient hyperthyroidism (which occurs in 1-2% of pregnancies)[3] are associated with elevated hCG levels during pregnancy[2]. It is important to distinguish gestational transient hyperthyroidism from Graves' disease because the course, fetal outcomes, management, and follow-up are different[3]. Graves' disease should be suspected if there is presence of goitre[1] and/or persistent abnormal thyroid function test result after 20th gestational week[5]. Gestational transient hyperthyroidism usually resolveed by then, when hCG levels decline[3].

The aim of this case report is to highlight the clinical presentation and transient phenomenon of gestational transient hyperthyroidism with hyperemesis gravidarum, and also to emphasize on the recommended management.

2. Case Report

A 30 year-old pregnant Indian lady, 14th week of pregnancy (Gravida 2, Para 1) was admitted to a hospital in Johor with frequent vomiting of more than 15 times daily, epigastric pain since her 10th week of pregnancy . The vomitus was mainly water and saliva as she was unable to tolerate orally, but she had two episodes of hematemesis in mid of April. She also complains of nausea, dizziness, lethargy, loss of appetite and weight, constipation, and right-sided headache. She denies symptoms suggestive of hyperthyroidism, such as fever, palpitation, agitation, diarrhea, and heat intolerance. She underwent caesarean section when giving birth to her first child due to breech birth. However she did not have hyperemesis gravidarum in her first pregnancy. She has no known medical illnesses and non-remarkable family history of thyroid disease.

Upon physical examination, the patient was afebrile, alert and conscious but dehydrated. Her pulse rate was 84 beats per minute with blood pressure of 117/70 mmHg. No hand tremors were observed. There was no conjunctiva pallor, but the patient was jaundiced. In addition, there were no eye signs of Graves' opthalmopathy and palpable goiter. Her lungs were clear and normal heart sounds (S1, S2) were heard with no murmurs. Her abdomen was soft but tenderness at right hypochondrium and epigastric region. The rest of the examinations were unremarkable.

Her laboratory test results showed consistent normocytic normochromic anemia, elevated bilirubin, ALT and AST, but low serum creatinine, serum potassium, magnesium and creatine kinase. The thyroid function test also shows evidence of thyrotoxicosis (elevated T4 and low TSH level) during 14th gestational week, but the values normalized during 15th gestational week as shown in Table I. However the TSH receptor antibodies, anitinuclear antibody test, antithyroglobulin antibody test and anitimicrosomal antibody test results show negative. Furthermore, the investigations for hepatitis A, B, C and the acid fast bacilli test, also show non-reactive.

Table 1. *Thyroid function test of patient*

	Reference value	14th gestational week	15th gestational week	17th gestational week
Free T4 (pmol/L)	10 - 20	45.00	18.40	13.56
TSH (miu/L)	0.2 - 4.0	0.090	0.030	0.776

The patient was given an intravenous drip of dextrose saline with potassium chloride throughout her stay in the hospital. Antithyroid medication was not introduced though her thyroid function showed hyperthyroidism. Her thyroid function test results normalize itself during her 15th gestational week. Her frequent vomiting was significantly reduced and was able to tolerate orally. Her general condition was stable and she was discharged after 4 weeks of hospital admission.

3. Discussion

3.1. Incidence and Prevalence

Hyperemesis gravidarum is defined as intractable excessive vomiting during pregnancy with onset before the 13th gestational week, usually the woman is unable to tolerate orally and requires intravenous hydration[1]. It is likely to be associated with hyperthyroidism secondary to the high hCG level. Various studies showed 0.3 – 1% prevalence of HG in pregnancy, with a mean onset during the 3rd gestational week, peaks in 11th–13th gestational week[2], and subsides after 14th-18th gestational week[3]. Hyperemesis gravidarum is possibly associated with signs of disturbed nutritional status (alterations in electrolyte balance, more than 5% weight loss, ketosis, acetonuria), neurological disturbances, retinal hemorrhage, liver and renal damage[2].

On the other hand, the most common thyroid disease in all pregnancies is Graves' disease (85 – 90%), while the secondly most common is gestational transient hyperthyroidism, which its incidence is 1–2% in all pregnancies[3,4]. Gestational transient hyperthyroidism is defined as firstly diagnosed hyperthyroidism in early pregnancy, which resolves spontaneously by the early second trimester of pregnancy, without evidence of autoimmune thyroid disease and physical findings associated with Graves' disease[4]. Gestational transient hyperthyroidism occurs up to two-thirds of women with hyperemesis gravidarum[1].

3.2. Pathophysiology of Gestational Transient Hyperthyroidism

The actual pathophysiology of gestational transient hyperthyroidism is still not completely understood, but it is strongly associated with human chorionic gonadotropin (hCG) level during pregnancy. In normal pregnancy, hCG is produced by the placenta in the first gestational week, its level peaks at 10th gestational week, then decreases and reaches a plateau by 20th gestational week[3]. HCG and TSH have identical α subunit, which may lead to cross reactivity between the increased level of hCG and TSH receptor, leading to stimulation of T3 and T4, in return causing negative pituitary feedback of TSH, resulting in high T3 and T4 level, but low TSH, especially in 8th–14th gestational week, when hCG level peaks during pregnancy[5]. Several clinical studies have reported high hCG level in women with hyperemesis gravidarum, and there are evidences showing that hCG level is positively correlated with the severity of vomiting and the degree of thyroid stimulation[1]. In addition, studies also showed that serum hCG is inversely proportionate to serum TSH[4]. A study showed that hCG level in women with gestational transient hyperthyroidism remained abnormally elevated for weeks during the second trimester and free T4 levels normalizes parallel with the decline of hCG level, thus supporting the role of hCG in the pathogenesis of gestational transient hyperthyroidism[1], as shown in Figure 1.Figure 1 shows the relationship between serum hCG and TSH[4].

Another explanation for gestational transient hyperthyroidism is that high estrogen level during pregnancy increases hepatic thyroid-binding globulin (TBG) synthesis, which reaches plateau during mid-gestation. The increased TBG level stimulates elevation of total T3 and T4 levels. The serum T4 level increases sharply between 6th-12th gestational week, and stabilizes around mid-gestation[5].

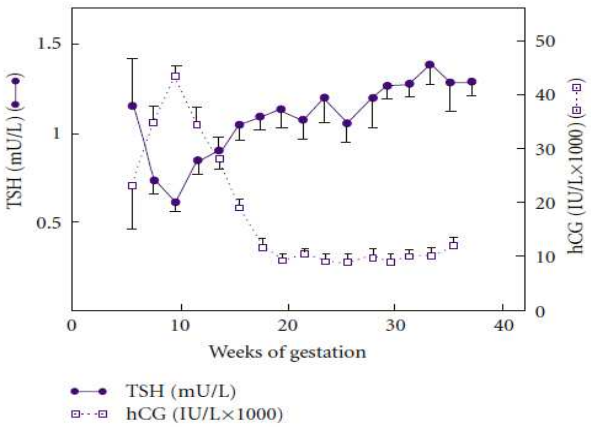

Figure 1. *Relationship between serum hCG and TSH*[4]

3.3. Clinical Features

Patients with hyperemesis gravidarum complicated with gestational transient hyperthyroidism usually complaint of nausea, vomiting and weight loss by gestational week 4-9, and present with tachycardia (secondary to dehydration), fine tremors and mild proximal weaknesses. In patients with high serum T3, they might present with shortness of breath, heat intolerance and palpitations. However, signs and symptoms suggestive of Grave's disease are absent[5,6]. A study showed that biochemical investigations in the early

presentation of women with gestational transient hyperthyroidism and hyperemesis gravidarum reveal hyponatremia, hypokalemia, mild hyperbilirubinemia, and mild to moderate elevation of aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) levels. However, viral hepatitis screening shows negative results among those with abnormal liver function test results. The free T4 level is found to be elevated in the first trimester, but normalized by 15th gestational week[1] and serum TSH in the first trimester could be as low as 0.03–0.08 mIU/L secondary to the thyrotropic activity of hCG[5].

Table 2.*Clinical presentations and investigation results of patients with hyperemesis gravidarum complicated with gestational transient hyperthyroidism*[4]

Medical History	Physical Examination	Laboratory Tests
- Absence of hyperthyroid symptoms prior conception - Similar history of vomiting in previous pregnancies - Family history of Hyperemesis Gravidarum - No previous history of thyroid disease	-No goiter -Absence of Graves' ophthalmopathy or dermopathy -No other physical findings such as vitiligo and Plummer's nails -Signs of dehydration	- Elevated free T4 - Suppressed or undetectable TSH - Negative thyroid antibodies: TPO and TRAb, - Transient electrolyte abnormalities - Abnormal liver function test results

3.4. Management

Women with hyperemesis gravidarum should be given supportive therapy with antiemetics, hydration, electrolyte replacement, and nutrition[6]. For those with hyperemesis gravidarum and gestational transient hyperthyroidism, anti-thyroid drugs (ATD) treatment is not recommended, as no benefit was supported by case reports and case studies. Gestational transient hyperthyroidism associated with hyperemesis gravidarum is of a transient nature where free T4 levels normalized by itself without ATD treatment[1]. Also, ATD treatment is poorly tolerated by patients, likely due to the persistent vomiting and metallic taste of ATD[4]. However, ATD treatment should be started if there is a persistence of hyperthyroid symptoms and thyroid function abnormalities after 18th-20th gestational weeks as this might indicate Graves' disease[6,7].

3.5. Nature Clinical Course of Gestational Transient Hyperthyroidism

In women with hyperemesis gravidarum and gestational transient hyperthyroidism, the onset of nausea is usually within the 4 gestational weeks, worsens by the 9th gestational week and completely resolves by 20th gestational week. The serum T4 is usually normalized by 15th gestational week, but serum TSH may remain suppressed until the end of second trimester[1,4]. No significant obstetrical complications had been found among these women, but the infants born have lower birth weight compared to normal infants[6].

4. Conclusion

In conclusion, gestational transient hyperthyroidism is a transient phenomenon which resolves itself by 20th gestational week. Therefore, ATD treatment is not indicated unless the diagnosis is uncertain. Supportive management is the recommended treatment for hyperemesis gravidarum, and hospitalization may be required in severe cases. The main message of this case report is that the recommended management of patients with hyperemesis gravidarum complicated with gestational transient hyperthyroidism should be supportive management only and ATD treatment is unnecessary as the transient phenomenon of hyperthyroidism in pregnancy resolves itself.

Author's Contribution

This case report was completed in collaboration between both authors: Cheau Wei Chin gathered information regarding the patient, obtained consent from the patient and written the first and final draft of the case report, while Dr. Aye Aye Myint shared the literature reviews and advised on proofreading. Both authors have approved the final draft. We would also like to thank the Director General of Health Malaysia for permission to publish this paper.

Consent

Consent for publication has been obtained from the patient.

Competing Interests

Both authors have declared that no competing interest was present.

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